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Influence of platelet hemostasis on QT interval dispersion in patients with chronic ischemic heart disease and COVID-19

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Coronavirus disease COVID-19 impairs platelet hemostasis, heart rate variability (HRV) and QT interval dispersion, increasing the risk of thromboembolic complications and cardiovascular mortality. Our study aimed to investigate the impact of COVID-19 on the interdependence of changes in platelet hemostasis and QT interval dispersion in patients with ischemic heart disease (IHD). We analyzed laboratory and instrumental results of 102 patients divided into 3 groups: group 1 consisted of IHD without COVID-19 patients (n = 32); group 2 − IHD in combination with COVID-19 (n = 35); group 3 − COVID-19 without IHD (n = 35). The control group included 30 conditionally healthy volunteers. Changes in platelet hemostasis were studied with laser aggregometry using the Born turbidimetric method and with light transmission fluctuation analysis using an assessment of spontaneous and induced aggregation: adenosine diphosphate (ADP), arachidonic acid, epinephrine, collagen, and ristomycin. The results of 24-hour Holter ECG monitoring were used to determine the QT interval dispersion. In patients of group 2, there was an increase in the degree, rate and time of spontaneous platelet aggregation, as well as a decrease in the degree, rate and time of platelet aggregation induced by epinephrine, a decrease in the rate of aggregation induced by arachidonic acid and ADP. The degree of aggregation was higher when using collagen and ristomycin. The QT interval duration and variability increased in all patients, especially in group 2. The time of spontaneous aggregation, as well as ADP- and collagen-induced aggregation, was directly correlated with the QT mode and mean. The standard deviation and coefficient of variation of QT were inversely related to the time of spontaneous aggregation, collagen- and ristomycin-induced and arachidonic acid-induced aggregation. The rate of aggregation did not affect the QT interval variability. Thus, patients with IHD and concomitant COVID-19 along with platelet hemostasis dysfunction exhibited signs of autonomic dysregulation and increased QT interval duration and variability. Careful consideration of platelet hemostasis characteristics and QT interval variability is recommended in the management of these patients.
Key words: chronic ischemic heart disease; COVID-19; QT interval dispersion; platelet hemostasis dysfunction; laser aggregometry.

INTRODUCTION

Despite the official end of the pandemic, COVID-19 remains a significant issue for modern medicine. Currently, there is a notable number of severe cases complicated by the development of acute respiratory distress syndrome, microthrombosis in the blood vessels of the lungs, kidneys, and heart, as well as deep vein thrombosis and pulmonary embolism. The prothrombotic changes in the platelet and plasma coagulation systems in the context of the new coronavirus infection have been specifically termed “coagulopathy associated with COVID-19.” The pathophysiology of the infection caused by SARS-CoV-2 is still insufficiently studied. The new β-coronavirus SARS-CoV-2 causes the development of thrombotic complications, especially in patients

with cardiovascular diseases and comorbidities. The impact of COVID-19 leads to significant changes at the molecular level, which can cause endothelial dysfunction and disrupt the balance in the systems of platelet and plasma coagulation, fibrinolysis, anticoagulant activity, and complement.

At the peak of the pandemic, it was found that the virus has a tropism not only for lung cells but also for other organs such as the heart, kidneys, and liver. This exacerbates pre-existing chronic diseases and worsens the condition of patients. Individuals with cardiovascular diseases have a greater tendency towards complications associated with COVID-19, as well as a higher level of associated mortality. Research into the pathophysiological aspects of autonomic nervous system (ANS) dysfunction in patients with ischaemic heart disease (IHD) who have recovered from COVID-19 is ongoing. During minor physical exertion, palpitations and shortness of breath may persist for up to a year (post-COVID syndrome). Holter ECG monitoring helps identify dangerous arrhythmias and conduction disturbances, as well as determine disorders of autonomic regulation and QT interval dispersion, which may be predictors of sudden cardiac death.

Since patients with COVID-19 exhibit dysregulation of QT interval dispersion, we hypothesised that changes in QT interval variability could be observed in patients with IHD during the acute phase. Furthermore, the parameters of QT interval dispersion in patients with IHD combined with COVID-19 have yet to be assessed. There is also a lack of scientific studies examining the relationship between QT interval dispersion indicators and parameters characterizing the state of platelet haemostasis in patients with IHD in the context of coronavirus disease. The aim of our study was to investigate the impact of COVID-19 on the interdependence of changes in the platelet haemostasis system and QT interval dispersion in patients with IHD.

METHODS

In a prospective study, clinical and instrumental data from 102 patients were analyzed, with the sample divided into three groups: Group 1 – IHD without COVID-19 (n = 32); group 2 – IHD in combination with COVID-19 (n = 35); group 3 – COVID-19 without CAD (n = 35). The control group consisted of 30 conditionally healthy individuals. The examination of patients in the study groups and individuals in the control group included a 12-lead ECG, 24-hour Holter ECG monitoring, and laser aggregometry (LA). The study was approved by the local Ethics Committee of the O.O. Bogomolets National Medical University (protocol No. 163 dated November 7, 2022). All patients provided informed consent before participating in the study.

In the control group, there were 23 men (77%) aged 47.1 ± 15.2 years and 7 women (23%) aged 42.8 ± 5.3. Group 1 included 32 patients with chronic IHD, with a mean age of 61.1 ± 12.2 years; there were 19 men (59%), and 10 individuals (31%) had diabetes mellitus, while 16 individuals (50%) had a history of myocardial infarction and underwent coronary angiography. Group 2 (IHD in combination with COVID-19) included 35 individuals aged 64.5 ± 11.7 years, with 25 men (71%), 6 individuals (17%) had diabetes mellitus, 14 individuals (40%) had a history of myocardial infarction, and coronary angiography was performed on 12 individuals (34%). According to computed tomography data, the degree of lung involvement was as follows: up to 25% – in 5 (14%), 25-50% – in 13 (37%), 50-75% – in 12 (34%), and 75% or more – in 5 (14%). Group 3 (COVID-19) included 35 patients aged 52.4 ± 11.5 years, with 27 men (77%), type 2 diabetes was found in 4 (11%) individuals, and lung involvement according to computed tomography was as follows: up to 25% – in 4 (11%), 25-50% – in 15 (42%), 50-75% – in 12 (34%), and 75% or more – in 4 (11%). When comparing groups based on most indicators, no significant differences were found, except for

cases of diabetes mellitus, which predominated in Group 1. All patients with IHD (groups 1 and 2) had hypertension.

According to the results of the 24-hour Holter ECG monitoring, using appropriate software (ECGpro®Holter, IMESC, Ukraine), QT dispersion indicators were evaluated: heart rate – (mean daily); SDNN – standard deviation of all NN intervals during the 24-hour Holter ECG monitoring (an integral indicator of HRV); QTc – duration of the QT interval corrected for heart rate; SDQT (NN) and SVQT (NN) standard deviation and coefficient of variation of the duration of all QT intervals during the 24-hour Holter ECG monitoring [9–12]. The methodology for studying platelet functional status was performed using LA by Born's turbidimetric method [13] and analysis of light transmission fluctuations (to assess the average size of aggregates) to study spontaneous and induced aggregation: with adenosine diphosphate (ADP), arachidonic acid, adrenaline, collagen, and ristocetin. A blood sample of 9 ml was taken from the patients into a tube containing a 3.8% sodium citrate solution according to the accepted methodology. Aggregation indicators were recorded on the BIOLA LA230-2 analyzer using the AGGR program. The results yielded an aggregogram. The degree of aggregation, speed, and time were determined from the light transmission curve.

Statistical processing of results was conducted using Statistica v. 14.0.0.1 software (TIBCO Software Inc., USA), and the Shapiro-Wilk test (W) was used to check for normality of distribution. In the case of non-Gaussian distribution, indicators were presented as median (Me), upper and lower quartiles. In the case of normal distribution, indicators were presented as mean value (M) and standard deviation (M ± SD). A comparison of central tendencies for two independent samples was performed using the Wilcoxon test. Multiple comparisons for three samples were conducted based on Kruskal-Wallis one-way analysis of ranks (Dunn's test). A difference was considered significant at $P < 0.05$.

RESULTS AND DISCUSSION

Indicators of QT interval variance according to 24-hour Holter ECG monitoring in patients in the study groups and control subjects are shown in Table 1.

Table 1. Indicators of QT interval dispersion by Holter ECG monitoring among patients with coronary heart disease and COVID-19 (Me) and [lower and upper quartiles]

Data	Control (n = 30)	Ischemic heart disease (group 1, n = 32)	Ischemic heart disease and COVID-19 (2 group, n = 35)	COVID-19 (3 group, n = 35)
Heart rate, bpm	60 [54; 80]	81[59; 101]*	79 [59;101]*	80 [64; 91]*
Average QT interval, ms	370 [326; 398]	398 [326; 436]	409 [367; 452]*	381 [367; 437]*
QT interval mode, ms	376 [321; 406]	395 [327; 442]	410 [325; 464]*	388 [357; 442]
Corrected QT interval, ms	394 [320; 450]	431 [378; 480]*	428 [142; 479]	430 [391; 502]*
The standard deviation of the variation in the duration of all QT intervals, ms	21 [13; 47]	36 [18; 80]*	41 [17; 80]*	29 [20; 69]*
Coefficient of variation of the duration of all QT intervals, %.	5,0 [2,8; 12]	8,6 [3; 13]*	9,2 [4; 22]*	8,0 [5; 11]*

Note: here and in Table 2, *$P < 0.05$ compared to the control group.

There was an increase in the duration of the QT interval and its variability (see Table 1). At the same time, the changes we found were most pronounced in the combination of coronary artery disease and COVID-19 for all characteristics of the QT interval studied. Given the likelihood of QT prolongation and, accordingly, the potential arrhythmogenic effect of some molecules used in the treatment of patients with COVID-19, in particular, azithromycin [15, 16], we note that this drug was prescribed to 5 (14%) and 4 (11%) patients in groups 2 and 3, respectively (P = 1,000). There was not a single case of hydroxychloroquine use among patients in these two groups.

The degree and time of spontaneous aggregation were greater in all patients compared to controls. An increase in its rate was seen in patients in groups 2 and 3. The highest value of the degree and speed of spontaneous aggregation was also noted in these groups compared with patients with isolated coronary artery disease. The time of spontaneous aggregation was longer in group 1 compared with group 2. The degree and rate of ADP-induced platelet aggregation were the lowest in group 2 compared with controls and other groups. In the 1st and 2nd groups, these indicators were lower than in the control group. The time of ADP-induced aggregation in the other groups did not differ significantly from the control. The degree of aggregation rate induced by arachidonic acid decreased in all groups compared with the control, the aggregation time did not differ significantly, except for patients in group 1, where it was the lowest compared with the control. The degree and rate of collagen-induced aggregation decreased in all groups, especially in group 1, and the aggregation time did not differ significantly between groups. The rate and degree of aggregation induced by adrenaline decreased in all groups compared with the control, especially in group 2. The aggregation time was the longest in group 3 compared with the control, and the shortest in group 2. In groups 1 and 3, the degree of aggregation induced by ristomycin decreased relative to the control. The rate of aggregation was higher in patients with COVID-19 (groups 2 and 3).

In patients with coronary artery disease, there was also a slight correlation between mean QT and the degree of aggregation induced by arachidonic acid, and an inverse correlation with the degree of aggregation induced by epinephrine. There was a direct correlation between MeanQT and the rate of aggregation induced by epinephrine. An inverse correlation was observed between collagen-induced aggregation time and SDQT(NN).

Among patients infected with SARS-CoV-2 (without signs of coronary artery disease), an inverse correlation was observed between the indicators of the functional state of platelet hemostasis: with heart rate and spontaneous aggregation rate, as well as between the rate of spontaneous aggregation, ADP-induced aggregation, and indicators of QT interval dispersion: QTc, SDQT(NN), SVQT(NN).

An interesting fact was the absence of a correlation between the degree of spontaneous aggregation and QT interval variability in patients with COVID-19. There was a direct correlation between the rate of spontaneous aggregation and SDQT(NN), as well as between the rate of ADP-induced aggregation and SVQT(NN). A slight inverse relationship was observed between the aggregation time induced by ristomycin and epinephrine and the QT interval variability: ModaQT, SDQT(NN), SVQT(NN). Direct correlations were found between the time of aggregation induced by ristomycin and epinephrine and the indicators reflecting the variability of the QT interval: MeanQT, SDQT(NN), SVQT(NN).

Among patients with concomitant IHD and COVID-19, the widest range of direct relationships of the degree of spontaneous aggregation was observed SDQT(NN) had a direct relationship with aggregation induced by epinephrine, but an inverse relationship with ristomycin. There was no relationship between QT interval variance and aggregation rate. Direct

relationships were observed between the time of spontaneous aggregation induced by collagen, ADP, as well as with ModaQT, ModaQT and Mean QT. The inverse relationships between the time of spontaneous aggregation, aggregation induced by collagen, arachidonic acid, ristomycin, and ModaQT, SVQT(NN), SDQT(NN) were investigated.

The variability of the QT interval had inverse relationships with the indices: MeanQT, QTc and between the degree of aggregation induced by ADP and ristomycin. MeanQT had a direct relationship with the rate of spontaneous aggregation induced by epinephrine and ristomycin, and an inverse relationship between it and aggregation induced by arachidonic acid.

Table 2: Indicators of the functional state of platelet hemostasis according to laser aggregometry in patients with ischemic heart disease (IHD) and COVID-19 (M ± SD)

Aggregation		Control (n = 30)	Ischemic heart disease (group 1, n = 32)	Ischemic heart disease and COVID-19 (2 group, n = 35)	COVID-19 (3 group, n = 35)
Spontaneous	Degree, %.	0,55±0,21	1,46±0,43*	2,74±9,74* P1-2<0,01	2,27±0,54* P1-3<0,01
	speed, %\min	1,17±0,31	1,94±0,59	2,54±0,56* P1-2<0,05	2,76±0,75 P1-2<0,05
	time, min	2,94±0,69	4,37±0,47*	4,11±0,77*	4,51±1,0*
ADP-induced	Degree, %.	60,7±6,2	48,7±20,6*	62,2±8,1 P1-2<0,01	62,2±4,8* P1-3<0,05
	speed, %\min	72,5±7,5	60,6±10,9*	60,3±9,3*	71,8±8,9 P1-3<0,05
	time, min	4,13±0,37	4,09±0,90	4,68±0,89	4,10±1,27
Induced by arachidonic acid	Degree, %.	69,9±9,4	12,7±4,9*	16,7±2,7*	23,6±3,8* P1-3<0,05
	speed, %\min	70,1±12,4	23,5±13,9*	46,0±10,9* P1-2<0,01	55,0±9,6* P1-3<0,01
	time, min	4,35±0,71	3,34±0,85*	4,54±1,02 P1-2<0,05	4,17±0,93 P1-3<0,05
Collagen-induced	Degree, %.	70,8±5,9	25,4±5,2*	63,5±14,3* P1-2<0,01	31,7±3,9* P1-3<0,05
	speed, %\min	82,5±10,3	15,7±8,6*	45,3±7,5* P1-2<0,01	40,8±14,5* P1-3<0,01
	time, min	4,32±0,82	4,31±0,47	4,67±0,80	4,55±0,76
Adrenaline induced	Degree, %.	68,7±7,9	40,2±11,1*	34,9±6,1* P1-2<0,05	38,1±4,9*
	speed, %\min	40,7±11,5	26,5±4,7*	23,8±4,7*	23,2±5,9*
	time, min	4,12±1,04	4,64±0,49	3,33±1,21 P1-2<0,05	5,04±1,01* P1-3<0,01
Ristomycin-induced	Degree, %.	63,2±9,8	40,9±12,5*	65,8±13 P1-2<0,01	55,3±9,1* P1-3<0,05
	speed, %\min	54,4±10,5	56,9±12,7	66,5±17,5*	68,6±15,9*
	time, min	4,67±0,40	4,11±0,78	3,93±0,83*	4,04±1,16

An inverse correlation was observed between the time of spontaneous aggregation and Mean QT, and between ModaQT and the time of aggregation induced by arachidonic acid.

Despite the known negative impact of COVID-19 in patients with cardiovascular disease [13-15], there is an urgent need to supplement the understanding of the pathophysiology of platelet hemostasis in SARS-CoV-2 infection, in particular, to study changes and interrelationships in the structural and functional state of platelet activity and HRV in patients with concomitant coronary heart disease.

Thus, in COVID-19, there is an increase in the activity and/or content of procoagulant proteins, such as factor VIII and von Willebrand factor, and changes in the activity of natural anticoagulants [15]. Pronounced procoagulant changes are observed in patients in the acute period of the disease, but they can persist after recovery, which requires antithrombotic prophylaxis [16]. Much of the research is devoted to the peculiarities of coagulation hemostasis, but the condition of platelets, which are no less important participants in hemostatic reactions than plasma coagulation factors in patients with COVID-19, is also of great interest. Platelets are nuclear-free fragments of megakaryocytes measuring 2-4 microns with a lifespan of about 8-10 days and play a key role in hemostasis and thrombosis reactions. In addition to providing primary hemostasis, they can synthesize protein, interact with blood and endothelial cells, and are a link between the hemostatic system and the immune system through the release of a number of cytokines and chemokines [2-8]. It has been shown that some patients with severe and moderate coronavirus infection have thrombocytopenia. However, a significant decrease in the platelet count to values that lead to the development of hemorrhagic complications (less than 30 x 10^9/L) is quite rare. The mechanism of thrombocytopenia in such patients is not fully understood. The decrease in platelet count is probably due to impaired hematopoiesis, increased destruction due to the influence of antiplatelet antibodies, and the presence of platelets in the vascular bed during the formation of microthrombi [12-16]. Some researchers have noted their hyperactivation in patients with severe and moderate COVID-19 when exposed to aggregation inducers such as thrombin, collagen, and ADP [15-18]. For 6 months or more after the disease, manifestations of post-COVID syndrome may be observed while maintaining an imbalance in immunological parameters, as well as in the plasma and platelet hemostasis system [12-18].

The results of a number of studies indicate that an increase in the variability of the QT interval on the ECG shows heterogeneity in ventricular repolarization processes, increasing the risk of life-threatening ventricular arrhythmias. Thus, according to the currently available data, an increase in the variance of the QT interval is a predictor of fatal ventricular arrhythmias, overall mortality, and sudden death of arrhythmic origin [4, 14]. Minguito-Carazo et al [16] found the prolongation of the QT interval in all patients with COVID-19, probably as a result of the prescribed treatment. Other authors claim that in SARS-CoV-2 infection, it was prolonged in only 20% of patients before treatment, although it increased by 72% with azithromycin and hydroxychloroquine, but no episodes of ventricular arrhythmia were recorded [15]. Our study demonstrated prolongation of the QT interval (mean and corrected) and an increase in its variability in all three study groups. Moreover, patients with combined IHD and COVID-19 had the most significant changes in these parameters compared with the values in the groups with an "isolated" course of both nosologies. At the same time, the frequency of azithromycin prescription in groups 2 and 3 was comparable, and none of the patients took hydroxychloroquine.

We have found that in patients with coronary artery disease in combination with COVID-19, the functional state of platelet hemostasis is significantly impaired: the degree, speed and time

of spontaneous platelet aggregation increases. At the same time, the degree, speed, and time of platelet aggregation induced by adrenaline decreased relative to ristomycin activation, with a downward trend. It should be noted that the rate of aggregation decreased when induced by arachidonic acid and ADP. The degree of aggregation was higher when using collagen and ristomycin. The aggregation time was shorter when induced by epinephrine. In addition, the QT interval dispersion, correlated with a number of platelet hemostasis parameters characterizing the dynamic mechanisms of regulation of the functional state of the hemostatic system.

The inverse relationship of the standard deviation of the QT interval variability and the QT variability coefficient with the degree of aggregation induced by ristomycin and the direct relationship with epinephrine was found. The time of spontaneous aggregation, as well as ADP- and collagen-induced aggregation, was directly correlated with the QT and mean QT modes. As for the standard deviation and coefficient of variation of the QT interval, an inverse relationship with the time of spontaneous aggregation, aggregation induced by collagen, arachidonic acid, and ristomycin was observed. The rate of aggregation did not affect the QT dispersion.

Given the association of disorders of autonomic regulation of heart rhythm and myocardial electrical alternation with an increased risk of life-threatening ventricular arrhythmias, as well as the data obtained during the pandemic, additional consideration of the characteristics of autonomic dysfunction is appropriate in the management of patients with IHD and concomitant coronavirus disease. This applies to both the acute period and the long-term follow-up after SARS-CoV-2 infection. It has been established that it can affect the reticular formation of stem structures and can change the functions of brain centers with a subsequent increase in central sympathetic potentials. This can impair the autonomic regulation of the heart and, accordingly, the state of blood rheology and platelet hemostasis [21, 22]. SARS-CoV-2 can infect and destroy, through toxin-mediated or immune action, extracardiac postganglionic neurons of the sympathetic nervous system, which further enhances the sympathetic effect on the hemostatic system. However, there are currently insufficient data to clearly explain this mechanism [20-23]. Also, the available data give us new insights into the impact of SARS-CoV-2 on the structural and functional aspects of platelet hemostasis [20-22], which raises additional questions about changes in spontaneous aggregation, as well as aggregation induced by epinephrine, ADP, collagen, arachidonic acid, and ristomycin, and their comprehensive assessment in the treatment of patients with COVID-19, including those with IHD.

These issues can be, at least partially, resolved through the use of innovative technologies, in particular, laser aggregometry to assess the functional state of platelet hemostasis [21-23].

CONCLUSIONS

1. In patients with coronary artery disease with concomitant COVID-19, a wide range of disorders of the functional state of platelet hemostasis was observed, including an increase in the degree and rate of spontaneous platelet aggregation, as well as a decrease in platelet aggregation induced by epinephrine.

2. The profile of IHD in combination with COVID-19, in contrast to the “isolated” course of both conditions, was characterized by a decrease in the aggregation rate when induced by arachidonic acid and ADP. The degree of aggregation was greater when using collagen and ristomycin, and the aggregation time was shorter when induced by epinephrine.

3. The duration and variability of the QT interval increased in chronic coronary artery disease and COVID-19, especially when they are combined.

4. There was an inverse relationship between the QT interval variance (standard deviation

and coefficient of variation) and aggregation induced by ristomycin and epinephrine. The time of spontaneous aggregation and ADP- and collagen-induced aggregation was directly correlated with the mode and mean QT. The standard deviation and coefficient of variation of QT were inversely related to the time of spontaneous aggregation induced by collagen, arachidonic acid, and ristomycin. The rate of aggregation did not affect the QT dispersion.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

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ВПЛИВ ТРОМБОЦИТАРНОГО ГЕМОСТАЗУ НА ДИСПЕРСІЮ ІНТЕРВАЛУ QT У ХВОРИХ З ХРОНІЧНОЇ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ ТА COVID-19

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При короновірусній хворобі COVID-19 порушується тромбоцитарний гемостаз, варіабельність серцевого ритму (ВСР) та дисперсія інтервалу QT, які підвищують ризик тромбоемболічних ускладнень і серцево-судинної смертності. Перспективним завданням є вивчення взаємозв'язків показників дисперсії QT і тромбоцитарного гемостазу у хворих на ішемічну хворобу серця (ІХС) у поєднанні з COVID-19. Метою нашого дослідження було дослідження впливу COVID-19 на взаємозалежність змін системи тромбоцитарного гемостазу та дисперсії інтервалу QT у хворих на ІХС. Проаналізовано лабораторно-інструментальні результати 102 пацієнтів, яких було поділено на 3 групи: 1-ша – ІХС без COVID-19 (n = 32); 2-га – ІХС у поєднанні з COVID-19 (n = 35); 3-тя – COVID-19 без ІХС (n = 35). До контрольної групи увійшли 30 умовно здорових волонтерів. Вивчали зміни тромбоцитарного гемостазу за результатами лазерної агрегатометрії турбідометричним методом Борна і за аналізом флуктуації світлопропускання з оцінкою спонтанної та індукованої агрегації: аденозиндифосфатом (АДФ), арахідоновою кислотою, адреналіном, колагеном, ристоміцином. Дисперсію інтервалу QT визначали за результатами 24-годинного холтерівського моніторування ЕКГ. У хворих 2-ї групи відмічено підвищення ступеня, швидкості і часу спонтанної агрегації тромбоцитів, а також зниження ступеня, швидкості і часу агрегації тромбоцитів, індукованої адреналіном, зниження швидкості агрегації при індукції арахідоновою кислотою і АДФ. Ступінь агрегації був більшим при використанні колагену та ристоміцину. У всіх пацієнтів збільшувалася тривалість та варіабельність інтервалу QT, особливо у 2-й групі. Час спонтанної агрегації, а також АДФ- і колагеніндукованої прямо корелював з модою QT і середнім QT. Стандартне відхилення та коефіцієнт варіації QT зворотно впливали на час спонтанної агрегації, колаген- та ристоміциніндукованої та індукованої арахідоновою кислотою. Швидкість агрегації не впливала на варіабельність інтервалу QT. Таким чином, пацієнти з хронічною ІХС та супутнім COVID-19 разом з дисфункцією системи тромбоцитарного гемостазу демонстрували ознаки автономної дисрегуляції та збільшення тривалості та варіабельності інтервалу QT. Додаткове врахування характеристик функції тромбоцитарного гемостазу та дисперсії інтервалу QT є доцільним у системі менеджменту таких пацієнтів.

Ключові слова: хронічна ішемічна хвороба серця; COVID-19; дисперсія інтервалу QT; дисфункція тромбоцитарного гемостазу; лазерна агрегатометрія.

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